# **Chronic Pain**



# ALEXANDRA SZABOVA AND KENNETH GOLDSCHNEIDER

Chronic Pain in Children Multidisciplinary Approach

> The Pain Physician The Psychologist The Physical Therapist The Nurse

> > The Consultant

**General Approach to Management** 

History
Physical Examination
Ancillary Data
Chronic Pain Conditions

Abdominal Pain
Headache
Complex Regional Pain Syndrome
Musculoskeletal and Rheumatologic Pain
Pain in Sickle Cell Disease, Trait, and Variants

Pain Pharmacotherapy

Nonsteroidal Antiinflammatory Drugs and Cyclooxygenase-2 Inhibitors

Opioids
Adjuvant Drugs

**Complementary Therapies** 

Summary

THE PRACTICING PEDIATRIC ANESTHESIOLOGIST sees chronic pain in one of three main venues: a child coming to the operating room for a procedure, after a request for a consultation from a colleague of another specialty, or when making acute pain management rounds. In this chapter, we focus on the essential approaches to children with chronic pain and provide guidelines to help the children and colleagues who request your assistance.

# Chronic Pain in Children

Chronic pain affects a large number of children.<sup>1</sup> Back pain has been reported in up to 50% of children by the mid-teens,<sup>2</sup> and abdominal pain occurs weekly in up to 17%.<sup>3</sup> Other conditions such as headaches, complex regional pain syndrome (CRPS), fibromyalgia, limb pain, chest pain, and joint pain are common and affect quality of life.<sup>4-7</sup>

Several chronic medical conditions are strongly associated with pain and blur the boundaries between acute and chronic pain treatment, including sickle cell disease, cystic fibrosis, epidermolysis bullosa,9 and cancer. These children require frequent hospitalizations, and their pain can be severe. Because the children present with pain in the hospital, treatment often follows the model for acute pain management based on medication use. However, psychosocial factors heavily influence the child's ability to cope and can improve or worsen the child's suffering, depending on personal and family factors. 10,11 It is appropriate to seek psychology, child life, and physical therapy consultations as part of the therapeutic plan. The ultimate goal for each of these medical conditions is to stabilize the child's condition and return her or him home. For many, the painful disease and dysfunction continue, and having a long-term plan that is integrated with acute management is vital.

# **Multidisciplinary Approach**

The model of care that appears to work optimally for children with chronic pain is one in which multiple disciplines are involved in developing a coordinated care plan. 4,12 In the outpatient setting, there is a pain physician, a psychologist, nurses, and a physical therapist. Sometimes, a neurologist or physiatrist may be involved. Anesthesiologists managing children with chronic pain should make use of these disciplines when recommending a plan of care. Advocating for the involvement of other therapeutic specialties can advance the patient's care beyond suggesting a regional block or medication.

# THE PAIN PHYSICIAN

The consulting anesthesiologist in an inpatient setting may be called on to provide care for one of three reasons. First, the patient may need a regional nerve block, such as an epidural steroid injection for magnetic resonance imaging-confirmed discogenic pain or epidural catheter placement to assist physical therapy. This consultation is fairly straightforward and is an extension of basic regional anesthesia principles. Second, a child who has been prescribed opioids chronically or other medications that have implications for anesthesia or postoperative pain management may present for consultation. The anesthesiologist must investigate possible drug interactions and determine which chronic medications have been prescribed; this approach is an extension of basic perioperative anesthesia skills. Third, a consultation may be requested to assess and diagnose the source of pain. This scenario is the most complex and requires taking a detailed history and performing a thorough physical examination. These children often require multidisciplinary care beginning with the initial evaluation and extending through treatment.

# THE PSYCHOLOGIST

Pain is more than just a physical phenomenon. It can cause and be worsened by stress, suffering, family dysfunction, social tension, anxiety, and depression.<sup>5,13</sup> Pain can disrupt almost any aspect of the life of the child or family. Family and school problems can worsen a painful condition and dramatically reduce a child's level of function. The family is always involved in the child's suffering and should therefore be included in the pain evaluation process.

Families often are wary about seeing a psychologist and are afraid of being stigmatized. It is important to emphasize that pain is what the child says it is, regardless of whether an obvious organic cause is identified. The child is being treated as a person, not just as the painful body part, and this approach should be emphasized for the child's family.

Psychology-based therapy includes relaxation training, bio-feedback, hypnotherapy, coping skills training, and psychotherapy. Biofeedback is a modality that trains the child to become more aware of his or her body, enhancing the sense of control over it. Therapies aimed at parental and familial aspects of the child's pain include teaching strategies for behavioral interventions (e.g., distraction), activity pacing, consistent discipline, coaching skills training, stress management, and occasionally, family therapy.

# THE PHYSICAL THERAPIST

Physical therapy is a crucial component of evaluating and treating chronic pain. The painful condition can cause loss of muscle strength and range of motion. Alterations in the use of a limb affect the biomechanics and daily function of the body. Children can become deconditioned and require a conditioning program to regain lost strength and stamina. These changes affect the original pain site and generate secondary pain problems that need to be addressed.

Physical therapy can benefit many painful conditions (e.g., myofascial pain improves with stretching and range-of-motion exercises) and is the cornerstone of treatment for others (e.g., chronic regional pain syndromes [CRPS]). Emphasizing self-reliance and responsibility for their own care is an important aspect of caring for adolescents. However, young children and older ones in pain cannot be expected to work aggressively at home without beginning with a structured program. Parental involvement is especially important for younger children, but the caretakers must be taught to be encouraging and supportive while not making them the child's taskmasters.

Therapies provided by physical therapy include stretching, strengthening, and reconditioning programs. Range-of-motion exercises and endurance training are also important. Aquatic therapy is very useful for children who cannot bear weight on lower limbs or have limited range of motion or strength. Massage, heat, and cold therapies are helpful adjuncts to increase functioning and enhance other physical therapy modalities.

Transcutaneous electrical nerve stimulation (TENS) is an effective, <sup>15</sup> low-risk, analgesic therapy that is usually provided under the guidance of a physical therapist. TENS is excellent for localized pain. The fact that it is portable, can be used discreetly, and has few side effects makes it attractive for use at school. Because tolerance to TENS can develop with prolonged use, children need to limit use to no longer than 2 hours at a time. They can take a break for an amount of time equal to the TENS use and then restart it.

# THE NURSE

Pain nurses play a major role in hospital-wide education of floor nurses regarding assessment and treatment of pain, including the use of epidural and patient-controlled analgesia (PCA) pumps. When starting to see chronic pain patients, the first personnel recruitment should be an advanced practice nurse who can be trained to triage, perform the initial evaluation and intake assessment, and assist with all subsequent pain-related issues that do not require the direct input of a physician.

# THE CONSULTANT

Anesthesiologists should be cognizant of their limitations and judiciously use of consultants to help make or confirm diagnoses and fashion the best treatment plan. Neurologists typically are well versed in headache management and in the use of many of the medications used for neuropathic pain. Physical medicine and rehabilitation specialists can assist in structuring a treatment plan for a variety of musculoskeletal pains and are accomplished in the treatment of spasticity.

# **General Approach to Management**

Most children with chronic, noncancer pain are adolescents who require special considerations in terms of their history and physical examination. Because they are between childhood and adulthood, their behavior can fluctuate broadly and often. It is important to address them directly but also involve the parents to the extent needed to obtain the relevant and complete history. The clinician should not try to be "cool" with the adolescent patient, because teenagers tend to find that approach condescending and will respond negatively. The examiner should instead find a point of common interest and use it to establish greater rapport.

Adolescents tend to be very image conscious. They may or may not want to discuss body functions such as defecation or menstruation, even when these functions are directly relevant to the problem. If patients seem uneasy with the questions, the physician should proceed in a straightforward manner, acknowledge their feelings, and reassure them that the information is needed to help them. When discussing these pediatric patients with parents, clinicians should use a phrase such as "children and young adults" rather than just "children" because even 12 and 13-year-olds like to think they are no longer children.

# **HISTORY**

The basic history focuses on the pain: location, duration, quality, intensity, aggravating and alleviating factors, associated symptoms, therapies that have been tried, and which tests have been performed and by whom. Pain intensity is often assessed by a 0 to 10 numeric rating scale for children older than approximately 8 years of age. The child must be asked about the current pain level and about the best and worst pain levels to obtain an idea of the pattern of pain and when it peaks. Quality descriptors include burning, sharp, aching, throbbing, tingling, numb, weird, and others; each may give a clue about the type of pain the child is experiencing. Odd descriptors, burning, and tingling suggest neuropathic pain; sharp, tight, and aching may indicate bony or muscular causes; throbbing suggests a vascular component; cramping or pain that comes in waves often suggests spasms of a muscle or hollow viscus.

A vital part of the chronic pain evaluation process is to look for *red flags*, which are signs or symptoms that may indicate a serious illness. Some of the red flag signs and symptoms for major pain types can be found in Tables 44-1, 44-2, and 44-3. For example, a child with back pain who also has weak legs and incontinence may have a tethered spinal cord. Headache that is worse in the morning and associated with vomiting suggests increased intracranial pressure. Back pain with loss of ankle jerk suggests compression of the S1 nerve root.

A complete pain evaluation comprises further history regarding medications, allergies, family history, and a thorough review of systems. Certain painful conditions, such as migraine headaches, <sup>16</sup> fibromyalgia, <sup>17</sup> irritable bowel syndrome, <sup>18</sup> and sickle cell disease, have a genetic basis. Knowing the family history can assist in making the diagnosis. The child sometimes may model his or her behavior after a family member. For example, if a

# TABLE 44-1 Red Flag Signs and Symptoms for Abdominal Pain

Persistent right upper or right lower quadrant pain

Dysphagia

Persistent or cyclic vomiting

Gastrointestinal blood loss

Family history of inflammatory bowel disease, celiac disease, or peptic ulcer disease

Pain that wakes the child from sleep

Arthritis

Nocturnal diarrhea

Involuntary weight loss

Deceleration of linear growth

Delayed puberty

Unexplained fever

Hepatosplenomegaly, masses, or perianal lesions

Bilious emesis

Costovertebral angle tenderness

# **TABLE 44-2** Red Flag Signs and Symptoms for Secondary Headache

Persistent vomiting

Focal neurologic signs

Meningeal signs

Unexplained fever

Increased intracranial pressure

Changes in behavior or mental status

Sudden onset of severe headache

Morning headaches

Headaches awakening the child from sleep

# TABLE 44-3 Red Flag Signs and Symptoms for Back Pain

Unexplained fever

Night sweats

Weight loss

Night pain

Constant pain

Bowel function changes

Urinary retention

Neurologic changes in legs: trouble walking, footdrop, weakness, loss of reflexes, sensory changes

parent has a "bad back" and is functionally compromised, the child also may complain of back pain. This does not mean the child is faking the complaints but simply patterning the behavioral response to pain after a model that he or she understands. Treatment can include reassurance, cognitive behavioral therapy, and gentle physical therapy to restore the child's functional ability and help him or her with any underlying issues. Family and social histories can be useful in fashioning a treatment plan in conjunction with the general history, physical examination, and relevant testing.

## PHYSICAL EXAMINATION

The physical examination should focus on the area of interest, but a brief general examination is also important. A full screening examination, including a neurologic examination, takes only a few minutes and can be combined with the social history. A systemic illness may manifest as a localized complaint; for example, diabetes can manifest as abdominal pain or leukemia as focal bone pain

When examining a child of the opposite sex, the physician should have a nonfamily observer of the same gender as the child present. Some children are very conscious of their bodies and may consider routine examination maneuvers as invasions of their privacy. The occasional child has a history of being abused and can be further traumatized by even a standard examination. Physicians can demonstrate examination techniques that may make the child uneasy. For example, a pinprick examination requires a needle or sharp object; the examiner should touch his or her own skin with a pin first to demonstrate that blood is not being drawn. Children are often fascinated by the deep tendon reflexes and usually have fun with that examination. Children with chronic pain often have had many examinations, and doing something a little different or fun can help them accept the current evaluation and enhance rapport.

# ANCILLARY DATA

By the time chronic pain patients have reached a pain clinic, they usually have undergone several investigative tests, and those data should be reviewed. After it becomes clear that there is no life-threatening illness, the focus should shift away from further testing. This is often a hard transition for families and children to accept, especially if no concrete diagnosis has been made to explain the pain. It is a challenge for them to embrace the thought that the pain itself is the disease rather than something that is still undiagnosed. Any study that may help to explain the pain or make a diagnosis that had not been entertained should be recommended. However, pursuing tests and imaging in an unfocused manner wastes resources and causes families to post-pone treatment while waiting for a diagnosis. Until the patient wholeheartedly endorses the treatment plan and becomes active in it, the child or adolescent's pain will continue unabated.

# **Chronic Pain Conditions**

Any part of the body can hurt, but in practical terms, several diagnostic clusters represent most pediatric pain conditions. The frequency and intensity of the pain can be striking. One study on the 3-month prevalence, characteristics, consequences, and provoking factors of chronic pain described the experience of 749 children and adolescents in one elementary and two secondary schools<sup>19</sup>: 83% experienced pain during the preceding 3 months. The leading sources of pain were headaches (60.5%,

also perceived as most bothersome), abdominal pain (43.3%), extremity pain (33.6%), and back pain (30.2%). Many subjects reported associated sleep problems, restriction in hobbies, and eating problems. School absenteeism reached 48.8% in the population with pain. The use of health care resources by children and adolescents with pain was extensive: 50.9% visited the physician's office, and 51.5% reported use of pain medication.

# **ABDOMINAL PAIN**

Abdominal pain is a major source of distress in children that causes anxiety and invites a large amount of testing. This painful condition, formerly referred to as recurrent abdominal pain, is now described as functional gastrointestinal disorders (FGIDs).<sup>20</sup> Specific criteria exist for the major categories so that FGIDs are no longer considered diagnoses of exclusion. The pain is thought to be caused by abnormal interactions between the enteric nervous system and central nervous system.<sup>21</sup> Research suggests that peripheral sensitization and abnormal central processing of afferent signals at the level of the central nervous system play roles in the pathophysiology of visceral hyperalgesia-a decreased threshold for pain in response to changes in intraluminal pressure.<sup>22</sup> The history and physical examination focus on excluding warning signs and symptoms of underlying disease (see Table 44-1).<sup>20,23</sup> The role for testing, endoscopy, and radiographic evaluation is limited.

Multidisciplinary treatment of FGIDs includes medication, psychological interventions, and education, which often need to be ongoing. The most important aspect of the treatment plan is to establish realistic goals, which frequently means return of function rather than complete elimination of pain. Although the literature for treatment is sparse, tricyclic antidepressants such as amitriptyline, nortriptyline, or doxepin have been used effectively for FGID-related pain. Anticonvulsants also are useful because they modify nerve conductivity and transmission. Antacids, antispasmodic agents, smooth muscle relaxants, laxatives, and antidiarrheal agents can be added to address symptoms. Data support the use of peppermint oil capsules in managing irritable bowel syndrome, although gastroesophageal reflux can be a limiting adverse effect.<sup>24</sup> Children with functional bowel disorders can have abnormal bowel reactions to physiologic stimuli, noxious stressful stimuli, or psychological stimuli (e.g., parental separation, anxiety). Children benefit from cognitive- behavioral therapy, coping skill development, biofeedback, hypnosis, and relaxation techniques (Table 44-4).<sup>25,26</sup>

# **HEADACHE**

Headaches can be categorized as primary or secondary. Primary headaches include migraine, tension, cluster, and trigeminal neuralgia headaches. Secondary headaches are those attributable to head and neck traumas; muscle spasms; vascular disorders; non-vascular intracranial disorders; infection; eye, ear, cranium, nose, sinus, and teeth or mouth diseases; homeostatic disturbances; and psychiatric disorders. Headaches represent one of the more poorly tolerated types of chronic pain, with greater medication use than for other types. Of 77 children with long-term headaches who were followed up to 20 years after the initial diagnosis, 27% were headache free, and 66% had improved.<sup>27</sup>

Migraines (especially migraine without aura) and tension-type headaches are the most common types of pediatric headaches. The prevalence of migraine ranges from 2.7% to 10%. It occurs more frequently in boys than girls between 4 and 7 years of age, and then the prevalence equalizes between 7 and 11 years of age.

# TABLE 44-4 Care Pathway for Abdominal Pain

## **Evaluation**

Medical examination

Behavioral medicine assessment

Review of records, treatments, history, and physical findings

Consultations with pediatrics, surgery, and gastroenterology specialists as indicated by presence of red flags; assessment may include laboratory testing, ultrasound, computed tomography or magnetic resonance imaging, endoscopy, lactose testing

# Treatment of Functional Gastrointestinal Disorders

Medications: tricyclic antidepressants; consider selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors; peppermint oil

Behavioral medicine: important and effective to de-medicalize therapy; de-emphasize testing and search for organic diagnoses; redirect focus to treatment and improved function

Physical therapy: not usually involved; trial of transcutaneous electrical nerve stimulation (TENS) if abdominal wall origin found

Other therapy:

Blocks are rare, except in palliative situation; celiac plexus with local anesthetic and steroid; epidural

Trigger point injections if abdominal wall trigger points found Acupuncture

Hypnosis

Meditation

Dietary management

After 11 years of age, three times more girls than boys have migraines.<sup>28,29</sup> Studies are not routinely recommended in the absence of focal neurologic findings. However, the practitioner must be alert to red flag signs and symptoms that warrant imaging and laboratory studies to rule out an underlying condition as a cause of the headaches (see Table 44-2).

There is a genetic component to migraine and chronic tension headaches; 50% to 77% of children with migraines have a positive family history for migraine headaches, especially on the maternal side. The clearest genetic link has been established for familial hemiplegic migraine. <sup>16</sup>

Children with frequent headaches often suffer from medication overuse headaches due to chronic or repeated use of overthe-counter analgesics. If possible, children should be weaned off analgesics gradually.

Treatments for migraine and tension-type headaches overlap greatly. Pharmacologic interventions can be divided in two types. In the first, abortive treatment focuses on stopping the acute headache. In the second, prophylactic therapy is indicated for patients with more than two headaches per month, for children with severe attacks, and for those with frequent headaches unresponsive to medication (Table 44-5).<sup>30</sup>

Older medications that have been used successfully to prevent headaches in adolescents include amitriptyline and trazodone. These medications tend to make children drowsy and are prescribed 30 to 60 minutes before bedtime each night. Younger children appear to respond well to the antihistamine cyproheptadine. Overall, few evidence-based recommendations can be made; the lack of randomized, controlled pediatric trials precludes an evidence-based recommendation.<sup>31</sup> However, the anticonvulsant topiramate is a promising medication for the prevention of migraine headaches.<sup>32-34</sup>

# TABLE 44-5 Care Pathway for Headaches

#### **Evaluation**

Medical examination

Behavioral medicine assessment

Physical therapy if neck or upper back tightness occurs

Review of records, treatments, history, and physical findings

Magnetic resonance imaging and neurology consultations as indicated by red flag signs and symptoms

## **Treatment**

Medications: tricyclic antidepressants, topiramate, trazodone, cyproheptadine

Behavioral medicine: biofeedback, relaxation, coping and pacing skills

Physical therapy: transcutaneous electrical nerve stimulation (TENS) unit on shoulders, posterior neck; stretching

Other therapy:

Yoga

Acupuncture

Meditation

Occasional neck trigger point injection or occipital nerve block

# **COMPLEX REGIONAL PAIN SYNDROME**

Type I and type II CRPS are different only in the presence of a documented nerve injury in type II (formerly called *causalgia*). Pain is an obligatory feature, often occurring alongside allodynia or hyperalgesia. There must be evidence at some time (not necessarily at the time of diagnosis) of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of pain. There are often features of a motor disorder such as tremor, dystonia, and weakness that sometimes lead to a loss of joint mobility. Nail and hair growth can also be affected. In the past, three distinct stages were described. However, it may be that there are phenotypic subtypes instead of stages.<sup>35</sup>

From a clinical standpoint, the typical pediatric CRPS patient is older than 10 years of age, Caucasian, female, and very active or a high achiever from an active family, and the child or adolescent presents with lower extremity pain. <sup>36</sup> A genetic predisposition is suggested by the clinical observation that CRPS is rare in the African American population. The rarity of CRPS in preadolescent children suggests a developmental aspect to its origin.

It is important to obtain a detailed history of the mechanism of trauma and the signs and symptoms. The examiner should specifically look for pain, allodynia, hyperalgesia, and hyperpathia. Edema and color changes do not have to be present at the time of diagnosis, but there should be a history of such changes in the recent past (Fig. 44-1). A complete neurologic examination includes testing muscle strength, reflexes, sensory responses (e.g., cold, touch, pinprick), capillary refill, temperature, and color differences. The physician should also look for deep tissue hyperalgesia. Occasionally, noninvasive or invasive testing may be helpful, but it is not sensitive or specific. These evaluations may include an electromyogram with nerve conduction velocity (EMG/NCV), quantitative sensory testing (QST), and quantitative sudomotor axon reflex testing (QSART) to detect small fiber dysfunction; thermography; and bone scans. Sympathetic ganglion blocks are not considered necessary for diagnosis, but they can be part of the therapeutic approach.

The therapeutic goal for CRPS is restoration of function. It may seem simple, but in daily practice, this may represent the

# **TABLE 44-6** Care Pathway for Complex Regional Pain Syndromes

#### **Evaluation**

Medical examination

Behavioral medicine assessment

Physical therapy assessment

Review of records, treatments, history, physical findings, and radiographic studies

## **Treatment**

Medications: tricyclic antidepressants, gabapentin, oxcarbazepine Behavioral medicine: very important, especially in refractory cases

Physical therapy: activate, range of motion, desensitization, strength training. Structured home program extremely important; may use transcutaneous electrical nerve stimulation (TENS) unit

# Other therapy:

Consider intravenous regional block for hand or foot Consider lumbar sympathetic block catheter and admission for structured program for lower extremity complex regional pain syndrome (CRPS) that is refractory despite best efforts of patient and family

Consider high thoracic epidural or continuous brachial plexus catheter for upper extremity CRPS



**FIGURE 44-1** Complex regional pain syndrome involves the patient's left foot and ankle. Notice the cyanosis and mottling. The affected foot was cool, and allodynia was prominent. Left foot toenails had not been trimmed in 3 months.

biggest challenge for the physician and the child. The therapeutic approach to the child with CRPS is multidisciplinary, with a focus on the psychosocial and physical aspects of the disease (Table 44-6). Education is important, and the information available on the Internet is ubiquitous, although it is often discouraging and not applicable to children with CRPS. No isolated treatment technique has been helpful for this condition. Children and physicians should follow an algorithm and adjust the therapeutic strategy every 4 weeks if the child does not respond satisfactorily to chosen measures.

The mainstay of CRPS treatment is physical therapy. However, the pain can be severe and disabling enough to prevent active participation by the child in the physical therapy program. Pharmacologic therapy is often initiated to facilitate physical therapy. Medications for neuropathic pain (described later) take time to titrate to effect. It is reasonable to use nonsteroidal antiinflammatory drugs (NSAIDs) and opioids for a short time until the primary medications take effect. The psychology team must play an active role in the overall treatment program. Psychosocial issues must be aggressively addressed. With physical therapy, psychology, and medications, most children achieve good results and disease resolution. In unusual refractory cases, for which interdisciplinary outpatient programs are insufficient, inpatient pain rehabilitation programs are recommended.

The role of interventional therapy in the treatment of CRPS is to alleviate the pain and provide the child with the opportunity to tolerate and advance in physical therapy. Sympathetic nerve blocks are widely used in adults although a systematic review revealed a lack of randomized, controlled trials to confirm the effectiveness of this approach in short-term and long-term pain relief.<sup>37</sup> Interventional therapies can be a double-edged sword, representing an easy solution that can demotivate the child from taking an active role in his or her physical therapy. However, pain may be too severe to allow physical therapy and thereby accelerate loss of function.

Several techniques enjoy popularity among pediatric pain specialists. For isolated limb CRPS, intravenous regional blockade with local anesthetic and adjuncts such as clonidine, ketamine, or ketorolac is performed. General anesthesia or deep sedation is frequently required because placement of intravenous catheters in the affected limb and inflation of the tourniquet are poorly tolerated. More invasive alternatives include placement of a lumbar sympathetic plexus catheter (Fig. 44-2) and a tunneled epidural catheter in the upper thoracic or lumbar area. The duration of infusion ranges from 3 to 5 days to as long as 4 to 6 weeks, and the procedure requires extensive logistical support. An alternative approach is to place a peripheral nerve catheter for a continuous block.<sup>38</sup> Spinal cord stimulation and intrathecal drug delivery are rarely used for pediatric CRPS due to the overall good prognosis with more conservative treatment and the continued growth of the skeleton, which can change the area of paresthesias in the case of spinal cord stimulators.

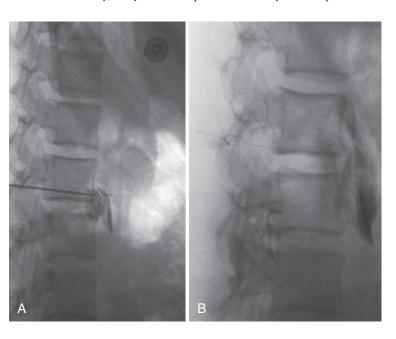
# MUSCULOSKELETAL AND RHEUMATOLOGIC PAIN

Musculoskeletal pain is a recognized problem in children and adolescents, and back pain commonly affects adolescents.<sup>39,40-42</sup> Although many factors are blamed for musculoskeletal pain (e.g., heavy backpacks, participation in sports, sedentary lifestyle, scoliosis, increased body mass index), only a few have been proved to contribute to musculoskeletal pain. According to one study, in more than half of cases the cause could not be identified, and only a minority of children had an underlying disease process (e.g., spondylolysis, infection, tumor, disk problem). Radiologic findings correlated poorly with the pain and failed to distinguish between individuals with pain and those without pain.<sup>42</sup> Selected red flags for back pain are provided in Table 44-3. A care pathway for the evaluation and treatment of back pain in children and adolescents is presented in Table 44-7.

A special group of children with musculoskeletal pain are those with rheumatologic diseases. Most children referred to the rheumatologist's office complain of musculoskeletal pain. Only some of them are diagnosed with a true rheumatologic disease; juvenile idiopathic arthritis is the most common form. Besides pain, the diseases often manifest as morning stiffness, fatigue, and sleep problems. The process may progress and cause joint deformities and destruction due to osteoporosis, with resulting growth abnormalities and functional disability. Management combines pharmacologic and nonpharmacologic interventions. The mainstay of therapy is the use of NSAIDs, acetaminophen, and rarely, opioids for severe breakthrough pain. The rheumatologist may prescribe agents such as methotrexate, cyclophosphamide, or systemic corticosteroids for severe flare-ups. Splints, physical therapy, and psychological interventions such as cognitive-behavioral therapy are often used.<sup>43</sup> Children with Ehlers-Danlos syndrome or other connective tissue disorders suffer from unstable joints that become very painful from repeated dislocations and mechanical stress.

Some young women present with fatigue, poor sleep, and pain or unusual tenderness in multiple sites. Fibromyalgia is more common in adolescents than expected, and it can be a significant problem. Therapy includes education, medications, and general restorative therapy, with a focus on aerobic reconditioning. Traditionally, tricyclic antidepressants and cyclobenzaprine have

**FIGURE 44-2** Lumbar sympathetic block. **A,** In the lateral view, the Tuohy needle is in the proper position. Notice the prepsoas spread of contrast agent. **B,** The dye spreads and clears due to injection of local anesthetic through the catheter. The catheter is tunneled and can be left in place for a week.



# TABLE 44-7 Care Pathway for Back Pain

#### **Evaluation**

Medical examination

Behavioral medicine assessment

Physical therapy assessment

Review of records, treatments, history, and physical findings

Consultation with specialists in orthopedics; magnetic resonance imaging or computed tomography, as indicated by history and examination findings

#### Treatment

#### Medications:

Tricyclic antidepressants

Muscle relaxants (e.g., baclofen, cyclobenzaprine)

Anticonvulsant (if radicular component)

Nonsteroidal antiinflammatory drug of choice

Cyclooxgenase-2 inhibitor for gastrointestinal or bleeding issues If disk disease with radicular pain is documented, up to three epidural steroid injections may be helpful

Behavioral medicine: biofeedback, coping skills, and relaxation techniques

# Physical therapy:

Stretching, postural rehabilitation, general reconditioning, and lifting techniques

Limit bed rest; reactivate

Transcutaneous electrical nerve stimulation (TENS)

Exercise program

# Other therapy:

Acupuncture

Yoga

Chiropractic (older patients, lumbar only)

Massage

Trigger-point injections

Additional modalities for specific indications include back bracing, surgery, bisphosphonate therapy

been used, and duloxetine and milnacipran are helpful in adults. 44,45 As with many chronic pain conditions, cognitive-behavioral approaches are valuable components of treatment. 46

Musculoskeletal pain is a particularly difficult problem in children with cerebral palsy.<sup>47</sup> Spasticity itself can be painful, and the daily stretching exercises are reported to be painful by many children. Some children with cerebral palsy are nonverbal, making assessment even more difficult. The parents or guardians can provide information about how the child expresses pain and how the pain manifests during daily life. If diaper changes seem to hurt, the practitioner should suspect hip or perineal pain. Pain after eating or a history of hard stools may point to constipation-based abdominal pain. A careful and sometimes staged examination is required. A thoughtful, empirical approach to therapy and judicious use of radiologic and laboratory evaluations can often lead to the diagnosis (Table 44-8).

# PAIN IN SICKLE CELL DISEASE, TRAIT, AND VARIANTS

Sickle cell disease is a hereditary disorder characterized by abnormal hemoglobin S (see Chapter 9). About 8% of African Americans carry the sickle gene. The homozygous form (sickle cell disease [HbSS]) manifests as a hemolytic anemia with unique vaso-occlusive features. The heterozygous form (sickle cell trait [HbAS]) is milder and manifests as a borderline anemia and rarely with vaso-occlusive features. Sickle cell/hemoglobin C disease

# **TABLE 44-8** Care Pathway for Nonverbal Patients

#### **Evaluation**

Medical examination

Often tricky; go slowly

May need more than one visit to complete the examination
Try to isolate body part during examination, to avoid generalized effect
Watch facial or vocal and parent reaction to each examination
maneuver

Behavioral medicine assessment: often not possible

Physical therapy assessment: often already engaged in therapy

Review of records, treatments, history, and physical findings

Video documentation: parent may be able to capture pain behaviors for examiner to view

#### [restment

Medications: often on multiple agents at baseline and coordination with other practitioners is important; apply general principles in choosing medications; long-acting opioid is sometimes beneficial for refractory musculoskeletal pain; watch for worsening of constipation.

Behavioral medicine: often not possible if patient's cognitive ability is too low, but the family sometimes can benefit because they carry a large burden when caring for children with multiple medical problems

Physical therapy: often already engaged; if not, engage for musculoskeletal pain or help therapist focus efforts of a particular region of the body

## Other therapy:

Nerve blocks can be used to identify painful areas, if more than one seems active

Rarely, a patient must be brought to the operating suite for an infusion of remifentanil to differentiate opioid responsiveness from potentially centralized or behavioral pain phenomena; the latter may respond to anticonvulsant therapy Intrathecal baclofen (and occasionally morphine)

Consider the areas for a standard distance

Surgical therapy for selected conditions

# Cautions

Site of pain is often unclear.

Do not forget to look in the ears.

If patient is spastic, strongly consider hip pathology (e.g., subluxation, bursitis, infection).

Constipation, gallbladder pain, and gastroesophageal reflux are possible.

These patients often require more testing than verbal patients.

Be careful with use of nonsteroidal antiinflammatory drugs because gastroesophageal reflux can be a problem and reporting abdominal pain as a signal of gastrointestinal side effects may not be possible.

(HbSC) has a clinical presentation similar to that of HbSS, but its vaso-occlusive episodes are fewer and usually less intense.

From a pain management perspective, the homozygous HbSS genotype manifests as acute pain attacks (e.g., pain crisis, vaso-occlusive episodes, acute chest syndrome) or as underlying chronic pain with acute exacerbations (e.g., avascular necrosis, vertebral collapse, joint involvement). Treatment frequently requires a multidisciplinary approach with close cooperation between the hematologist, psychologist, and pain physician. Most of the episodes can be managed at home with NSAIDs or acetaminophen, supplemented with opioids such as codeine or oxycodone or with tramadol. In severe cases, children often are hospitalized and treated with intravenous opioids, although they should be gradually weaned off the opioids as the primary process improves. For episodes of localized, hard-to-control pain or if acute chest syndrome develops, epidural analgesia can provide

# TABLE 44-9 Care Pathway for Sickle Cell Disease

## **Evaluation**

Medical examination

Behavioral medicine assessment: may be limited to social support in acute setting

Review of records, treatments (need opioid exposure history for dosing), and history

Hematology almost always directly involved, with focused evaluation

# Treatment of Vaso-occlusive Episodes

Medications: opioid (often requires basal infusion for the first days); nonsteroidal antiinflammatory drug; consider neuropathic medication for hyperalgesia

Behavioral medicine: can be helpful, although learning techniques in the acute setting may be difficult; introducing this modality early in life may be more helpful

Physical therapy: transcutaneous electrical nerve stimulation (TENS) for localized pain

Other therapy:

Regional anesthesia may be helpful.

Strongly consider thoracic epidural for acute chest crisis.

## **Treatment of Chronic Problems**

Medications: may involve chronic opioids; otherwise follows treatment of particular pain condition

Behavioral medicine: per particular pain condition; early involvement may reduce need for hospitalizations

Physical therapy: per particular pain condition; may have joint, bone, and deconditioning issues from recurrent vaso-occlusive episodes

excellent relief.<sup>49</sup> Rarely, children require opioid maintenance with long-acting preparations of morphine or oxycodone (Table 44-9). Hyperalgesia over the affected area suggests peripheral or central sensitization, although the role for neuropathic medications is undefined.

# Pain Pharmacotherapy

Pain treatment has received less study in children than adults, as it is true for much pediatric pharmacologic therapy. In the absence of U.S. Food and Drug Administration (FDA)–approved indications and experimental data, off-label use of many medications used to treat chronic pain is common. In this situation, the decision to use a particular medication is most often based on extrapolation from adult literature, expert consensus, applied theory, and clinical judgment (see Chapter 6). Three categories of medications are available for consideration: nonopioid analgesics (i.e., NSAIDs and acetaminophen), opioid analgesics, and a broad spectrum of adjuvant analgesics, including anticonvulsants, antidepressants, muscle relaxants, local anesthetics, N-methyl-D-aspartate (NMDA) receptor antagonists,  $\alpha_2$ -agonists, and corticosteroids.

# NONSTEROIDAL ANTIINFLAMMATORY DRUGS AND CYCLOOXYGENASE-2 INHIBITORS

NSAIDs come from various chemical groups (e.g., salicylates, propionic acid, oxicams, naphthylalkalones, fenamates). The mechanism of action is inhibition of cyclooxygenases (COXs) at the prostaglandin H<sub>2</sub> synthetase enzyme. COX-1 is constitutive and always present, and COX-2 is inducible and produced in the body under proper conditions. NSAIDs have different

selectivities for COX-1 or COX-2; selective COX-2 inhibitors have predominant action on inducible COX-2. The benefit of selective blockade is decreased risk of gastrointestinal bleeding. Celecoxib is the only selective COX-2 inhibitor available in the United States.

The analgesic and antiinflammatory actions of NSAIDs exhibit a dose-dependent response until they reach maximum effect; beyond which there is no further benefit of dose increase (i.e., ceiling effect). Unlike opioids, there is no development of physical dependence or tolerance with NSAIDs.

The choice of NSAID is empirical and based on clinical judgment. If the child provides a history of good response to a particular NSAID, we tend to continue the same medication or adjust the dose. If the response is inadequate, we select a different medication until we find an effective one. In children with a history of gastrointestinal adverse effects, we prescribe combination preparations with protective agents (e.g., misoprostol) or a histamine<sub>2</sub> (H<sub>2</sub>) receptor or proton pump inhibitor, or we switch to a selective COX-2 inhibitor. Preexisting renal disease and disorders that reduce actual or effective intravascular volume vastly increase the risk for renal toxicity, and NSAIDs must be used cautiously in these situations.

## **OPIOIDS**

The use of opioids for treating chronic nonmalignant pain has been associated with many myths and controversies. Their use in the past was reserved for children with acute and cancer-related pain. In selected cases, with appropriate monitoring, opioids can improve quality of life and functional capacity without significant risk of addiction, tolerance, and toxicity. However, a history of substance abuse (mainly in adolescent and young adult populations) and a family member with substance abuse and a dysfunctional social situation are red flags for opioid prescribing.

Opioid agonists are used almost exclusively; agonistantagonists have less popularity because of their ceiling effect and the potential to precipitate withdrawal when administered alongside a pure agonist. We typically use opioids in two scenarios. The first features opioids as a bridge while titrating other classes of medications to effect or while awaiting physical therapy or an intervention to exert its effect. In the second scenario, we use opioids as maintenance analgesics in carefully selected children (e.g., chronic musculoskeletal pain in a child with cerebral palsy, children with juvenile rheumatoid arthritis or Ehlers-Danlos syndrome). Medication is titrated in increments toward the main goals of optimal (although rarely complete) pain relief, improved function, and minimal adverse effects. Escalations are seen usually with exacerbations of the primary disease process. Common opioid adverse effects that occur with long-term use can be found in Table 44-10.

A special medication in this group is methadone. Besides being an opioid agonist, methadone is also reasonably effective in controlling neuropathic components of pain. There are a few exceedingly important caveats for its use. It has a long half-life and presents a risk of accumulation leading to sedation and respiratory depression. The usual 1:1 methadone to morphine equianalgesia ratio does not work for dose conversion. The greater the dose of opioid being converted, the more skewed the conversion ratio; the methadone to morphine ratio ranged from 1:2.5 to 1:14.3 in one study.<sup>50</sup> Because of the long half-life, dose adjustments should be made no more frequently than every 5 days. A unique adverse effect of methadone among opioids is its potential to prolong the QT interval and modestly increase

# TABLE 44-10 Opioid Side Effects Associated with Chronic Use

## With Development of Tolerance

Cognitive impairment

Itching

Miosis

Nausea

Prolonged reaction time

Respiratory depression

Sedation

Urinary retention

# Without Development of Tolerance

Constipation

# Side Effects with Long-Term Use

Hypogonadism Immunosuppression

the dispersion of repolarization on the electrocardiogram.<sup>51</sup> Because the dispersion of repolarization is less than 100 msec, it remains unlikely that methadone can trigger torsades de pointes.

When a child who is taking long-term opioids presents in the operating room, a thorough medication history is essential for developing a perioperative plan. If the child has not taken a morning dose of opioid, that dose should be replaced by the intravenous route to avoid withdrawal. It is essential to convert the home medication into morphine equivalents, and the daily dose of home opioids should be provided as a baseline, with all further dosing being in addition to the baseline, to avoid pain at the time of emergence. Because of tolerance to long-term opioids, larger doses than usual may be required, and it is advisable (as in all children) to titrate to comfort in the immediate postoperative period and use the amount required to achieve optimal analgesia. Opioid consumption during the perioperative period may be more than three times that observed in patients not taking chronic opioids. Sparing use of opioids in the perioperative period results in poor pain management and withdrawal phenomena.52,53

# **ADJUVANT DRUGS**

# Anticonvulsants

Anticonvulsant medications have been widely used in the pharmacologic treatment of chronic pain since the 1960s. Often referred to as membrane stabilizers, anticonvulsants work on neural receptors, ion channels, and nerve conductivity. They modify the level of excitatory and inhibitory neurotransmitters and activation of nerve cells. They are most effective in controlling neuropathic pain. First-generation agents (e.g., carbamazepine) have been used less often due to significant adverse effects, and they have been replaced by second-generation agents that have a better adverse effect profile.

Therapeutic effect is achieved with all membrane stabilizers by gradual titration. The purposes of this approach are to avoid development of adverse effects by allowing enough time for the child to develop tolerance (mainly to sedation) and to find the lowest effective dose for the child. The treatment course usually lasts 3 to 6 months. At the end, the child is gradually weaned off the medication in reverse order of its titration. Although weaning is not necessary to prevent seizures, rapid discontinuation may result in pain and in sleep or mood disturbances. Gradual weaning allows rapid re-escalation in case the pain begins to return in children for whom the pain has been controlled but

not completely eliminated. In that case, we would determine the child's minimal effective dose. If pain recurs, we continue medication for 3 to 6 months longer.

Although use of anticonvulsants for pain in children represents an off-label use and studies are lacking (even for adults), this class of medications is a mainstay of therapy for selected pain conditions in children. The choice of drug is based on thoughtful consideration and expert consensus, as with all therapies for which randomized, controlled trials are lacking.

# Gabapentin and Pregabalin

Gabapentin is an anticonvulsant with a complex mechanism of action. Its name is deceiving; gabapentin does not interact with the  $\gamma$ -aminobutyric (GABA)-ergic system. It binds to the  $\alpha_2$ -delta subunit of the voltage-dependent calcium channel<sup>54</sup> and reduces the release of glutamate in the dorsal horn of the spinal cord. This leads to decreased production of substance P, less activation of  $\alpha$ -amino-3-hydroxy-5-methylisoxazole-4-propionate (AMPA) receptors on noradrenergic synapses, decreased transmitter release, and decreased neuronal activity. This mechanism is shared by gabapentin and pregabalin.

Gabapentin is usually a drug of first choice due to good tolerability, minimal adverse effects, and positive clinical experiences. Besides sedation, patients can retain sodium and water, develop peripheral edema, and gain weight. In teenagers, gabapentin can cause mood swings, irritability, and suicidality. Despite these concerns, we use gabapentin frequently after a detailed explanation and discussion with the patient and parents. We use two titration schedules. For younger children, the target dose is 10 to 15 mg/kg/dose three times per day. In older children weighing more than 60 kg, we use adult-type titration to effect. Gabapentin does not have to be adjusted in liver failure patients because it is not metabolized by the liver; however, the dosage needs to be adjusted in children with compromised renal function. Pregabalin is chemically related to gabapentin but has fewer adverse effects and a significantly faster titration schedule. It is approved for postherpetic neuralgia, diabetic neuropathy, and fibromyalgia in adults; experience in children is growing.

# **Topiramate**

Best studied for the treatment of migraine headaches, topiramate can be applied to the full spectrum of neuropathic pain states.<sup>33</sup> Because a unique adverse effect is appetite suppression, we may choose it for a patient with neuropathic pain who is concerned about weight gain. Topiramate has carbonic anhydrase–inhibiting properties and can result in metabolic acidosis and lead to renal stones in some cases.

# Oxcarbazepine

Oxcarbazepine is the second-generation relative of carbamazepine and has potential for the treatment of neuropathic pain states. Although rare, Stevens-Johnson syndrome can occur with oxcarbazepine and with several other anticonvulsants. Hyponatremia also may occur in addition to adverse effects common to anticonvulsants, such as sedation, difficulty concentrating, ataxia, and mood instability.

# Carbamazepine, Valproic Acid, and Phenytoin

The effectiveness of carbamazepine, valproic acid, and phenytoin has been discussed elswhere. <sup>56</sup> Carbamazepine has proved effective in the treatment of trigeminal neuralgia, spasticity in multiple sclerosis, and spinal cord injury (compared with tizanidine).

Phenytoin has been used alone or in combination with buprenorphine for cancer pain, and it has provided good pain relief in more than 60% of patients.

Despite their effectiveness, the use of these medications is limited because of the possibility of serious adverse effects. For carbamazepine and phenytoin, adverse effects include liver and renal toxicity (regular laboratory tests are necessary), aplastic anemia, Steven-Johnson syndrome, and a syndrome of inappropriate secretion of antidiuretic hormone (SIADH)-like picture. Valproate lacks renal side effects but can cause pancreatitis.

# **Antidepressants**

Two major groups of antidepressants are used in the treatment of chronic pain: tricyclic antidepressants (TCAs) (e.g., amitriptyline, nortriptyline, desipramine, doxepin, imipramine) and the newer selective serotonin reuptake inhibitors (SSRIs) (e.g., fluoxetine, paroxetine) and serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g., venlafaxine, duloxetine, milnacipran).<sup>57</sup> The efficacy of TCAs in the treatment of neuropathic pain has been confirmed in meta-analyses.<sup>58,59</sup> The doses required to control chronic pain are usually less than those used in the treatment of depression. The effectiveness of antidepressants has been demonstrated in neuropathic and nonneuropathic pain such as fibromyalgia and low back pain.

When prescribing antidepressants, we recommend vigilance about the potential increase in suicidal ideation and attempts in adolescents and young adults. We inform patients and families in detail to ensure that they will communicate with us about such ideation. We refer patients at greater risk for psychiatric comorbidity to a psychologist for evaluation before prescribing this class of medications.

# Tricyclic Antidepressants

The major limiting factor in prescribing TCAs is their adverse effects. Onset of adverse effects can be reduced by slow dose escalation, as is done with anticonvulsants. The most frequent side effect is sedation, which is often beneficial in chronic pain patients who have difficulties sleeping. We prescribe the drug to be taken at bedtime. It is important to monitor the child in the mornings for carryover sedation. In such cases, it is reasonable to decrease the dose or encourage the child to take the medication earlier in the evening. Because of the anticholinergic effects of TCAs, children often notice a dry mouth and may experience constipation, urinary retention, or weight gain.

TCAs prolong the cardiac QT interval, which can cause a lethal arrhythmia. We obtain a careful history of cardiac symptoms and conduction abnormalities in the child and family members. It is reasonable to order a baseline electrocardiogram to rule out congenital prolonged QT interval before initiation of therapy. Because concomitant use of SSRIs, SNRIs, or tramadol can decrease the seizure threshold in children with a seizure disorder, their simultaneous use is discouraged. Amitriptyline and nortriptyline are the most commonly used medications of this group. The usual starting dose for both medications is 5 to 10 mg orally at night, which is increased to 20 or 25 mg at night 1 week later. Analgesic effects can be seen in 1 to 3 weeks, as with antidepressants effects. Nortriptyline is a metabolite of amitriptyline, with similar utility for pain but less sedation. If top-range dosing is required, periodic electrocardiographic monitoring for QTc changes is suggested.

# Selective Serotonin and Norepinephrine Reuptake Inhibitors

Venlafaxines starting dose is 37.5 mg/day in adults, which can be increased by 37.5 mg every week up to 300 mg/day. Adverse

effects include headaches, nausea, sweating, sedation, hypertension, and seizures. If the dose is less than 150 mg/day, the effects are mostly serotoninergic. If it exceeds 150 mg/day, the effects are mixed serotoninergic and noradrenergic. Duloxetine has anti-depressant effects and analgesic effects for neuropathic pain, fibromyalgia, and back pain. 45,57,60 It is usually started at 20 to 60 mg daily to a maximum dose of 120 mg/day. The major adverse effects are nausea, dry mouth, constipation, dizziness, and insomnia. Use of both medications in younger children is best left to those who prescribe the medications frequently because dosing has not been well established in the pediatric age group.

# Muscle Relaxants

Muscle relaxants are frequently used as an adjunct to other medications (mostly NSAIDs) in patients with myofascial pain.

# Cyclobenzaprine

Cyclobenzaprine is a centrally acting muscle relaxant. Its major adverse effects are somnolence, dizziness, and asthenia. The usual starting dose is 5 mg at night, which can be increased to 10 mg after 5 to 7 days unless the child has difficulties awakening in the morning. The dose can be escalated up to 10 mg three times per day.<sup>61</sup>

# Baclofen

Baclofen is one of the most powerful centrally acting muscle relaxants. It interacts with the GABA<sub>B</sub> receptor subtype. It is usually indicated in patients with spasticity such as children with cerebral palsy or multiple sclerosis. In children 2 to 7 years old, the daily dose is 10 to 15 mg, divided into two or three doses. The dose can be escalated every 3 days by 5 mg to a maximum dose of 40 mg/day. In children older than 8 years of age, the maximum dose is 60 mg/day. Baclofen is one of a few medications approved for intrathecal administration by implanted pumps and is usually administered to children with spasticity (e.g., cerebral palsy, spinal cord injury).

# Tramadol

Tramadol is a unique analgesic. It is a very weak  $\mu$ -receptor opioid agonist. It also blocks monoamine reuptake in the central nervous system (similar to antidepressants). For the latter reason, tramadol is a popular analgesic for neuropathic pain, especially for controlling paresthesias, allodynia, and touch-evoked pain. The likelihood of tolerance or development of dependence is small, although it has been reported. Despite its weak opioid properties, sudden discontinuation of tramadol can cause withdrawal symptoms.

The doses used for chronic pain vary from 25 mg up to 100 mg four times per day (400 mg/day maximum).<sup>62</sup> The dose should be limited in renally impaired children with creatinine clearance less than 30 mL/min up to a maximum of 200 mg/day and in those with impaired liver function up to 100 mg/day.

Common adverse effects include nausea, vomiting, sedation, constipation, diarrhea, dizziness, headache, seizures, and hallucinations. Rare side effects include orthostatic hypotension, syncope, and tachyarrhythmia.

# Local Anesthetics, α<sub>2</sub>-Adrenergic Receptor Agonists, Topical Agents, and N-Methyl-d-Aspartate Receptor Antagonists

Many drugs are used in the treatment of chronic pain, and they have a wide array of mechanisms of action. Oral medications with local anesthetic properties such as mexiletine have been used in the treatment of neuropathic pain in patients with CRPS. The  $\alpha_2$ -adrenergic receptor agonist clonidine finds its application in the same arena. It is used orally, as a transdermal patch, or added to local anesthetic solutions in intravenous regional techniques. The major limiting factor in the use of these drugs is their adverse effect profile, which includes hypotension, sedation, bradycardia, and nausea (especially with mexiletine).  $\alpha_2$ -Adrenergic agonist blocking properties are also part of the mechanism of action of the muscle relaxant tizanidine.

The topical agent capsaicin, derived from hot chili peppers, is also helpful in managing neuropathic pain, but its application can cause a burning sensation where applied, which is often poorly tolerated. The topical lidocaine patch has been effective in the controlling symptoms of postherpetic neuralgia and has been used for localized myofascial pain, hyperpathia, and allodynia in other neuropathic conditions. Pharmacokinetic studies in adults have found minimal lidocaine blood concentrations, suggesting a large margin of safety, 4 although similar studies have not been carried out in children.

NMDA receptor antagonists such as ketamine, amantadine, or dextromethorphan have anecdotal evidence supporting their utility in the treatment of neuropathic pain. It is also thought that NMDA receptor antagonists exert an opioid-sparing effect. An important limiting factor of the broader use of ketamine in the treatment of chronic pain symptoms is the potential for psychotropic side effects.

# **Complementary Therapies**

Alternative therapies have appealed to patients for a long time. Because traditional medical therapies have a high failure rate, patients continue to search for better treatments. Many types of therapies are useful in treating chronic pain. As a consultant, the anesthesiologist should consider suggesting some of these therapies when they seem appropriate. TENS and biofeedback have been discussed earlier.

Acupuncture and its derivative, acupressure, originated in China and constitute an important part of traditional Chinese medicine (Fig. 44-3). In acupuncture, the body energy or qi (pronounced *chi*) circulates in body meridians and collaterals. Meridians and collaterals are pathways that represent body organ



FIGURE 44-3 Acupuncture needles in situ.

systems called the Zang-Fu organs. In Chinese medicine, pain is caused by obstruction in the circulation of qi in these channels due to multiple causes. Acupuncture has been used in acute and chronic pain conditions such as neck and back pain, dental pain, musculoskeletal and arthritic pain, CRPS, migraine, facial pain, and fibromyalgia. The data from randomized, controlled trials is controversial or insufficient to support or deny efficacy of acupuncture.<sup>65</sup>

# Summary

The pediatric anesthesiologist may be called on to assist with the care of a child or adolescent with chronic pain. The basic tenets of care apply, and a careful history and focused physical examination remain key components of the evaluation. Determining that the child is not being physically harmed by the painful condition (i.e., ensuring safety) is the first step, followed by focused diagnostic evaluation and therapy. Treatment for all but the simplest painful conditions employs multiple disciplines in a coordinated attack on the pain. The input of psychologists is a prominent part of chronic pain management, and psychological treatment is not a sign of psychiatric disease or malingering but a tool that can be powerful and effective. Physical therapy and judicious use of medications round out the approach to most chronic pain problems in children. The occasional use of interventional modalities and opioids is warranted, but success is limited if the problem is viewed in a unidimensional manner. Many patients benefit from alternative approaches to therapy, and these disciplines can be used in a prudent fashion to expand the range of therapies that can be recommend.

# ANNOTATED REFERENCES

Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JA, et al. Pain in children and adolescents: a common experience. Pain 2000;87:51-8.

This survey article describes the prevalence of chronic pain in children, which is a much more common problem than previously recorded in the general population.

Ripamonti C, Groff L, Brunelli C, et al. Switching from morphine to oral methadone in treating cancer pain: what is the equianalgesic dose ratio? J Clin Oncol 1998;16:3216-21.

This is an intriguing discussion about the conversion ratio between morphine and methadone. It explodes the commonly held belief (seen in so many opioid conversion tables) that the two opioids are equianalgesic.

Stanton-Hicks M, Baron R, Boas R, et al. Complex regional pain syndromes: guidelines for therapy. Clin J Pain 1998;14:155-66.

The article outlines the multidisciplinary approach to complex regional pain syndromes (CRPS). Multidisciplinary treatment is not just for children with CRPS

Turk DC. Clinical effectiveness and cost-effectiveness of treatments for patients with chronic pain. Clin J Pain 2002;18:355-65.

The author takes a look at the big picture. Blocks make us money; comprehensive treatment makes patients better.

Wilder RT, Berde CB, Wolohan M, et al. Reflex dystrophy in children: clinical characteristics and follow-up of seventy patients. Am J Bone Joint Surg 1992;74:910-9.

The classic paper describes complex regional pain syndrome in children, its treatment, and patient outcomes. Its observations hold up today.

# **REFERENCES**

Please see www.expertconsult.com.

# **REFERENCES**

- Perquin CW, Hazebroek-Kampschreur AA, Hunfeld JA, et al. Pain in children and adolescents: a common experience. Pain 2000; 87:51-8.
- 2. Burton AK, Clarke RD, McClune TD, Tillotson KM. The natural history of low back pain in adolescents. Spine 1996;21:2323-8.
- 3. Hyams JS, Burke G, Davis PM, et al. Abdominal pain and irritable bowel syndrome in adolescents: a community-based study. J Pediatr 1996;129:220-6.
- Chalkiadis GA. Management of chronic pain in children [comment]. Med J Aust 2001;175:476-9.
- Kashikar-Zuck S, Goldschneider KR, Powers SW, Vaught MH, Hershey AD. Depression and functional disability in chronic pediatric pain. Clin J Pain 2001;17:341-9.
- Hunfeld JA, Perquin CW, Bertina W, et al. Stability of pain parameters and pain-related quality of life in adolescents with persistent pain: a three-year follow-up. Clin J Pain 2002;18:99-106.
- Hunfeld JA, Perquin CW, Duivenvoorden HJ, et al. Chronic pain and its impact on quality of life in adolescents and their families. J Pediatr Psychol 2001;26:145-53.
- 8. Koh JL, Harrison D, Palermo TM, Turner H, McGraw T. Assessment of acute and chronic pain symptoms in children with cystic fibrosis. Pediatr Pulmonol 2005;40:330-5.
- Fine JD, Johnson LB, Weiner M, Suchindran C. Assessment of mobility, activities and pain in different subtypes of epidermolysis bullosa. Clin Exp Dermatol 2004;29:122-7.
- Scharff L, Langan N, Rotter N, et al. Psychological, behavioral, and family characteristics of pediatric patients with chronic pain: a 1-year retrospective study and cluster analysis. Clin J Pain 2005; 21:432-8.
- Lynch AM, Kashikar-Zuck S, Goldschneider KR, Jones BA. Psychosocial risks for disability in children with chronic back pain. J Pain 2006;7:244-51.
- 12. Turk DC. Clinical effectiveness and cost-effectiveness of treatments for patients with chronic pain. Clin J Pain 2002;18:355-65.
- Varni JW, Rapoff MA, Waldron SA, et al. Chronic pain and emotional distress in children and adolescents. J Dev Behav Pediatr 1996;17:154-61.
- 14. Stanton-Hicks M, Baron R, Boas R, et al. Complex regional pain syndromes: guidelines for therapy. Clin J Pain 1998;14:155-66.
- Rushton DN. Electrical stimulation in the treatment of pain. Disabil Rehabil 2002;24:407-15.
- 16. Ophoff RA, Terwindt GM, Vergouwe MN, et al. Familial hemiple-gic migraine and episodic ataxia type-2 are caused by mutations in the Ca<sup>2+</sup> channel gene CACNL1A4. Cell 1996;87:543-52.
- Buskila D, Neumann L. Genetics of fibromyalgia. Curr Pain Headache Rep 2005;9:313-5.
- 18. Pace F, Zuin G, Di Giacomo S, et al. Family history of irritable bowel syndrome is the major determinant of persistent abdominal complaints in young adults with a history of pediatric recurrent abdominal pain. World J Gastroenterol 2006;12:3874-7.
- Roth-Isigkeit A, Thyen U, Stoven H, et al. Pain among children and adolescents: restrictions in daily living and triggering factors. Pediatrics 2005;115:e152-62.
- Rasquin A, Di Lorenzo C, Forbes D, et al. Childhood functional gastrointestinal disorders: child/adolescent. Gastroenterology 2006; 130:1527-37.
- Kellow JE, Azpiroz F, Delvaux M, et al. Applied principles of neurogastroenterology: physiology/motility sensation. Gastroenterology 2006;130:1412-20.
- Grundy D, Al-Chaer ED, Aziz Q, et al. Fundamentals of neuro-gastroenterology: basic science. Gastroenterology 2006;130: 1391-411.
- 23. Di Lorenzo C, Colletti RB, Lehmann HP, et al. Chronic abdominal pain in children: a technical report of the American Academy of Pediatrics and the North American Society for Pediatric

- Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr 2005;40:249-61.
- 24. Grigoleit HG, Grigoleit P. Peppermint oil in irritable bowel syndrome. Phytomedicine 2005;12:601-6.
- Robins PM, Smith SM, Glutting JJ, Bishop CT. A randomized controlled trial of a cognitive-behavioral family intervention for pediatric recurrent abdominal pain. J Pediatr Psychol 2005;30: 397-408
- Youssef NN, Rosh JR, Loughran M, et al. Treatment of functional abdominal pain in childhood with cognitive behavioral strategies. J Pediatr Gastroenterol Nutr 2004;39:192-6.
- Brna P, Dooley J, Gordon K, Dewan T. The prognosis of childhood headache: a 20-year follow-up. Arch Pediatr Adolesc Med 2005; 159:1157-60.
- 28. Abu-Arefeh I, Russell G. Prevalence of headache and migraine in schoolchildren. BMJ 1994;309:765-9.
- 29. Abu-Arafeh IA, Russell G. Epidemiology of headache and migraine in children. Dev Med Child Neurol 1993;35:370-1.
- 30. Ferrari MD. Migraine. Lancet 1998;351:1043-51.
- 31. Lewis D, Ashwal S, Hershey A, et al. Practice parameter: pharmacological treatment of migraine headache in children and adolescents: report of the American Academy of Neurology Quality Standards Subcommittee and the Practice Committee of the Child Neurology Society. Neurology 2004;63:2215-24.
- 32. Bussone G, Usai S, D'Amico D. Topiramate in migraine prophylaxis: data from a pooled analysis and open-label extension study. Neurol Sci 2006;27(Suppl 2):S159-63.
- Hershey AD, Powers SW, Vockell AL, LeCates S, Kabbouche M. Effectiveness of topiramate in the prevention of childhood headaches. Headache 2002;42:810-8.
- 34. D'Amico D, Grazzi L, Usai S, Moschiano F, Bussone G. Topiramate in migraine prophylaxis. Neurol Sci 2005;26(Suppl 2):S130-3.
- Bruehl S, Harden RN, Galer BS, et al. Complex regional pain syndrome: are there distinct subtypes and sequential stages of the syndrome? Pain 2002;95:119-24.
- Wilder RT, Berde CB, Wolohan M, et al. Reflex dystrophy in children: clinical characteristics and follow-up of seventy patients.
   J Bone Joint Surg Am 1992;74:910-9.
- Cepeda MS, Carr DB, Lau J. Local anesthetic sympathetic blockade for complex regional pain syndrome. Cochrane Database Syst Rev 2005;(4):CD004598.
- Lee BH, Scharff L, Sethna NF, et al. Physical therapy and cognitivebehavioral treatment for complex regional pain syndromes. J Pediatr 2002;141:135-40.
- Kristjansdottir G. Prevalence of self-reported back pain in school children: a study of sociodemographic differences. Eur J Pediatr 1996;155:984-6.
- 40. Leboeuf-Yde C, Kyvik KO. At what age does low back pain become a common problem? A study of 29,424 individuals aged 12-41 years. Spine 1998;23:228-34.
- Ehrmann Feldman D, Shrier I, Rossignol M, Abenhaim L. Risk factors for the development of neck and upper limb pain in adolescents. Spine 2002;27:523-8.
- 42. Jones GT, Macfarlane GJ. Epidemiology of low back pain in children and adolescents. Arch Dis Child 2005;90:312-6.
- 43. Anthony KK, Schanberg LE. Pediatric pain syndromes and management of pain in children and adolescents with rheumatic disease. Pediatr Clin North Am 2005;52:611-39, vii.
- 44. Kyle JA, Dugan BD, Testerman KK. Milnacipran for treatment of fibromyalgia. Ann Pharmacother 2010;44:1422-9.
- Arnold LM, Rosen A, Pritchett YL, et al. A randomized, doubleblind, placebo-controlled trial of duloxetine in the treatment of women with fibromyalgia with or without major depressive disorder. Pain 2005;119:5-15.
- Kashikar-Zuck S, Swain NF, Jones BA, Graham TB. Efficacy of cognitive-behavioral intervention for juvenile primary fibromyalgia syndrome. J Rheumatol 2005;32:1594-602.

- 47. McKearnan KA, Kieckhefer GM, Engel JM, et al. Pain in children with cerebral palsy: a review. J Neurosci Nurs 2004;36:252-9.
- 48. Ballas SK. Pain management of sickle cell disease. Hematol Oncol Clin North Am 2005;19:785-802.
- 49. Yaster M, Tobin JR, Billett C, et al. Epidural analgesia in the management of severe vaso-occlusive sickle cell crisis. Pediatrics 1994;93: 310-5.
- 50. Ripamonti C, Groff L, Brunelli C, et al. Switching from morphine to oral methadone in treating cancer pain: what is the equianalgesic dose ratio? J Clin Oncol 1998;16:3216-21.
- Krantz MJ, Lowery CM, Martell BA, Gourevitch MN, Arnsten JH. Effects of methadone on QT-interval dispersion. Pharmacotherapy 2005;25:1523-9.
- 52. de Leon-Casasola OA, Myers DP, Donaparthi S, et al. A comparison of postoperative epidural analgesia between patients with chronic cancer taking high doses of oral opioids versus opioid-naive patients. Anesth Analg 1993;76:302-7.
- 53. Rapp SE, Ready LB, Nessly ML. Acute pain management in patients with prior opioid consumption: a case-controlled retrospective review. Pain 1995;61:195-201.
- 54. Sills GJ. The mechanisms of action of gabapentin and pregabalin. Curr Opin Pharmacol 2006;6:108-13.
- Coderre TJ, Kumar N, Lefebvre CD, Yu JS. Evidence that gabapentin reduces neuropathic pain by inhibiting the spinal release of glutamate. J Neurochem 2005;94:1131-9.
- Wiffen P, Collins S, McQuay H, et al. Anticonvulsant drugs for acute and chronic pain. Cochrane Database Syst Rev 2005;(3): CD001133.

- Maizels M, McCarberg B. Antidepressants and antiepileptic drugs for chronic non-cancer pain. Am Fam Physician 2005;71:483-90.
- McQuay HJ, Tramer M, Nye BA, et al. A systematic review of antidepressants in neuropathic pain. Pain 1996;68:217-27.
- Collins SL, Moore RA, McQuay HJ, Wiffen P. Antidepressants and anticonvulsants for diabetic neuropathy and postherpetic neuralgia: a quantitative systematic review. J Pain Symptom Manage 2000;20: 449-58.
- Prakash A, Lobo E, Kratochvil CJ, et al. An open-label safety and pharmacokinetics study of duloxetine in pediatric patients with major depression. J Child Adolesc Psychopharmacol 2012;22:48-55.
- Romano TJ. Fibromyalgia in children; diagnosis and treatment. W V Med J 1991;87:112-4.
- Rose JB, Finkel JC, Arquedas-Mohs A, et al. Oral tramadol for the treatment of pain of 7-30 days' duration in children. Anesth Analg 2003;96:78-81.
- 63. Davies PS, Galer BS. Review of lidocaine patch 5% studies in the treatment of postherpetic neuralgia. Drugs 2004;64:937-47.
- Gammaitoni AR, Alvarez NA, Galer BS. Safety and tolerability of the lidocaine patch 5%, a targeted peripheral analgesic: a review of the literature. J Clin Pharmacol 2003;43:111-7.
- 65. Eshkevari L. Acupuncture and pain: a review of the literature. AANA J 2003;71:361-70.